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Advancing a Multilevel Framework for Epidemiologic Research on Asthma Disparities*

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Our understanding of asthma epidemiology is growing increasingly complex. Asthma outcomes are clearly socially patterned, with asthma ranking as a leading cause of health disparities among minority and low socioeconomic groups. Yet, the increasing prevalence and marked disparities in asthma remain largely unexplained by known risk factors. In the United States, asthma disproportionately affects nonwhite children living in urban areas and children living in poverty. Low socioeconomic status (SES), ethnic minority group status, and residence in an inner-city environment are closely intertwined in the United States, making it a challenge to fully disentangle the independent effects of each of these characteristics on asthma morbidity. In addition, studies show geographic variation in asthma outcomes across large cities and neighborhoods within cities that cannot be explained by economic factors alone. Although more limited data are available, studies in rural areas also suggest the stratification of risk based on SES and the proportion of minorities. Among low-SES areas, those with predominantly minority, segregated populations seem especially burdened. Marginalized populations of lower socioeconomic position are disproportionately exposed to irritants (*eg*, tobacco smoke), pollutants (*eg*, diesel-related particles), and indoor allergens (*eg*, cockroach and mouse allergen). Moreover, these marginalized individuals may also live in communities that are increasingly socially toxic, which, in turn, may be related to the increased experience of psychosocial stress that may influence asthma morbidity. Epidemiologic trends suggest that asthma may provide an excellent paradigm for understanding the role of community-level contextual factors in disease. Specifically, a multilevel approach that includes an ecological perspective may help to explain heterogeneities in asthma expression across socioeconomic and geographic boundaries that, to date, remain largely unexplained. Traditionally, asthma epidemiology has focused on individual-level risk factors and family factors. Far less attention has been given to the broader social context in which individuals live. A multilevel approach that explicitly recognizes the embedding of asthma within its biological, psycho-socioeconomic, environmental, and community contexts, is likely to provide a better understanding of asthma disparities at different stages in the life course. Is it simply asthma disparities or is it social disparities in asthma? ***(CHEST 2007; 132:757S–769S)***

Key words: air pollution; asthma disparities; environmental justice; housing; indoor allergens; stress; tobacco smoke; violence

Abbreviations: ND = neighborhood disadvantage; PAH = polycyclic aromatic hydrocarbon; SES = socioeconomic status

While asthma prevalence and the associated morbidity are increasing in the United States and worldwide,[1] the increase is far from uniform. In the United States, for instance, these trends disproportionately affect nonwhite children living in urban areas and children living in poverty. Many studies have indicated that racial and ethnic minority groups and persons of lower socioeconomic status (SES) have higher asthma prevalence than their white, non-Hispanic, and more affluent counterparts. Inner-city communities and minority communities experience an excess burden of asthma hospitalizations and mortality that is out of proportion to the increase in asthma prevalence seen in these communities. Despite improved preventive asthma medications, asthma death rates have been increasing

over the last few decades, especially in urban communities with lower SES and largely minority populations.[2–6] More recent evidence suggests that the epidemiology of asthma is still more complex. In the United States, a graded association between SES and asthma prevalence, morbidity, and mortality has been demonstrated.[7–11] Moreover, data from the United States demonstrate significant geographic variations in asthma outcomes among large cities[12] and neighborhoods within cities.[2,3,13] These and other studies documenting the observed disparities in the US asthma burden have been well summarized elsewhere.[1,14]

Although not a universal finding across studies, racial/ethnic differences seem to exist independent of SES.[15,16] In the United States, asthma prevalence, hospitalization, and emergency department use declined with increasing income for non-black children, but not for black children.[17] Another US study[18] found that the lifetime prevalence of asthma was 2.1 times higher in blacks than whites, despite the fact that subjects were of similar middle and higher economic status. Although the authors proposed that their findings may be attributable to biological differences based on race, several considerations argue against this explanation. Most notably, the observed increase in asthma and the growing disparities documented between ethnic minorities and white populations have occurred over 1 to 3 decades, which is too rapid a change to be plausibly attributed to genetic mutation or change. These data do suggest that other unique characteristics among minority populations beyond simply economic well-being may impact their health.

It is worth noting up front that while much of the work to date (as well as much of this overview) has tended to focus on urban living, the relatively few studies[1] conducted in the United States that have examined the prevalence of asthma in rural vs urban areas have yielded inconsistencies. As discussed below, such geographic differences have generally been attributed to differential exposure to large domestic animal sources of allergens and endotoxins. Yet, very high prevalence rates of asthma have been demonstrated in rural Connecticut, particularly in low-income regions with predominantly minority populations.[19] While rural asthma rates may be related, in part, to differences in exposures among farm-reared vs non-farm-reared individuals, as a 2005 Midwest study proposes,[20] we need studies that more fully examine sociodemographic factors[21] and barriers to health-care access[22,23] that are unique to rural areas both in general and among ethnic subpopulations living in different regions of the United States[24] that may influence rural asthma outcomes. This is not insignificant, as people living in rural areas make up 20% of the US population, and rural areas have higher percentages of people living in poverty and lacking health insurance coverage compared to other regions in the United States. In contrast to urban demographics, where concentrated poverty typically impacts ethnic minority populations, many poor rural poor populations are primarily white.

The relative importance of urban residence, low SES, or minority (particularly black and Hispanic) status as independent risk factors for increased asthma morbidity and morality remains controversial. These social indicators remain tightly woven together in the United States. A more nuanced approach that considers both social and physical factors that covary with lower SES and minority-group status (*eg*, differential environmental exposures, residential segregation, psychological stress, housing quality, and social capital) that mediate the effects of living in low-SES neighborhoods is needed to tease these relationships apart. The preceding empirical evidence, while it should in no way should be interpreted as evidence for the social causation of asthma, highlights the marked socioeconomic patterning of the disease, and as such provides a foundation to view asthma within its social context. Such a view underscores why measuring health disparities with reference to informative socioeconomic and demographic groupings,[25] as opposed to examining health disparities without any reference to their socioeconomic or demographic characteristics,[26] is critical to how we conceptualize the issue of what causes asthma or leads to increased morbidity.

The causes of the excess burden of asthma in inner-city, lower income, and ethnic minority communities are not fully understood, and it is likely that

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multiple factors play contributing roles. To date, research attempts to explain these disparities have been nested in our current understanding of asthma risk (*ie*, those related to physical environmental factors). These are briefly discussed below, and the reader is referred to more extensive reviews for further detail.[1,14] However, ecologic views on health recognize that individual-level health risks and behaviors have multilevel determinants, in part influenced by the social and geographic context within which subjects live.[27–31] These social conditions can be biologically embedded parallel to how we think about physical environmental exposures and their effects on health.[32] The convergence of theoretical and methodological approaches from traditionally distinct areas of scholarship (*eg*, sociology, psychology, economics, social epidemiology, geography, asthma epidemiology, environmental sciences, environmental justice, and genetics) is needed to guide further research related to the environmental causes of asthma disparities.

How Well Do Current Paradigms Explain Disparities?

Various explanations exist in the current literature to account for the social disparities in asthma. These are outlined below.

Physical Environmental Exposures in the Home and Community

Hygiene Hypothesis

The so-called *hygiene hypothesis* grew out of observations in the late 19th and early 20th centuries that hay fever and wheezing illnesses appeared to be diseases of more affluent urban areas, compared with rural farming areas.[33,34] To explain these patterns, hypotheses have evolved to include the following: (1) small families, later birth order, and the use of day care; (2) less exposure to respiratory infection in early childhood; (3) a reduction in endotoxin or other farm-related exposures; (4) a change in microbial colonization of the infant's large bowel through diet or antibiotic use; (5) reduced exposure to parasites; or (6) reduced exposure to large-domestic animal sources of allergens.[1] The basic underlying mechanism suggested is that early-life infections and exposure to bacterial products such as endotoxin related to increased microbial load in homes where pets are kept may activate the T-helper type 1 immune response pathway, inhibiting the development of the T-helper type 2 responses involved in allergy.[35–38] However, the relevance to the urban disparities seen in the United States is unclear. Inner-city children do not necessarily live in more hygienic conditions or experience fewer infections than children from other socioeconomic groups. Inner-city children do not, in general, experience the protective exposure to farm animals that protect against asthma and atopy in European populations.[35,39,40] Moreover, it has been suggested that endotoxin levels may be higher in inner-city areas and that urban children may indeed have increased exposure to siblings and other children in daycare environments, although this has not been systematically tested.[1] The relevance of the hygiene hypothesis to the excess asthma seen in the inner city remains uncertain and is the subject of ongoing investigations.

Indoor Allergens

The relationship between asthma and hypersensitivity to aeroallergens has been documented in cross-sectional studies[41] and, more recently, in prospective studies.[8,42] IgE-mediated hypersensitivity to environmental allergens is present in most children and young adults with asthma, and exposure to allergens appears to be involved in the initial development of asthma as well as the exacerbation of existing asthma.[43] Cockroach allergen is an important, well-described allergen that is associated with asthma, especially in low-income urban communities[44–46] (see Burkart et al[14] for a detailed more recent review). Cockroach allergen is more frequently encountered in urban homes than in rural homes. Studies also have demonstrated that rat and mouse allergen are commonly found in urban housing and have suggested that increased asthma morbidity may be associated with rodent sensitization.

Early-life exposure to aeroallergens may influence polarization of the immune system toward an atopic phenotype and predisposition to wheeze expression in the first year of life.[47] The mechanisms underlying early sensitization to allergens that may underlie increased asthma risk are not unique to asthma in the inner city. Rather, the specific indoor allergens and intensity of exposures encountered in the inner city differ from those found in other environments.[48–51] It has also been demonstrated[52] that the concentrations of allergens in urban homes have a wide range and are associated with race/ethnicity and SES. For example, in the northeastern United States, high levels of *Bla g* 1 and *Bla g* 2 in house dust are associated with low SES, African-American race, and urban residence.

Moreover, it seems from recent data that children of lower SES communities are more likely to be responsive to multiple allergens. A national sample of US

children[53] demonstrated that African-American and Mexican-American children were significantly more likely than white children to be sensitized to allergens relevant to asthma. It may be that in addition to being at increased risk of exposure to multiple allergens, the interaction with other factors that are disproportionately distributed in lower income groups (*ie*, pollutants and toxicants, and psychological stress) prime the immune system toward an enhanced response to these environmental allergens.[54] Indeed, our group recently reported increased asthma risk among urban children exposed to both elevated levels of traffic-related air pollution and chronic psychosocial stress operationalized as violence exposure.[55]

At the same time, policy, economics, and sociology literature confirm that housing conditions, and therefore the environmental exposures that come along them, are strongly related to the economic status of the people who live there.[56] Socioeconomic deprivation results in higher percentages of income devoted to rent and more substandard conditions. Environmental psychologists and social scientists, among others, have suggested that housing also has a significant subjective emotional dimension.[57,58] While the more subjective or emotional response to one's housing can be positive, serving as a reflection of positive personal identity, a site for the exercise of control, and a source of social status,[58] they can also be associated with psychological distress. A number of subjective housing characteristics have been linked to adverse psychological outcomes.[59] Future studies considering the role of housing on asthma disparities need to consider physical factors as well as the social and psychological dimensions of housing.[60]

Asthma Disparities and Diesel Particles

The increase in respiratory allergic diseases in urban areas has also been linked to air pollution. Laboratory studies[61] have confirmed the epidemiologic evidence that the inhalation of some pollutants adversely affect lung function in asthmatic patients. The most abundant air pollutants in urban areas with high levels of vehicle traffic are respirable particulate matter, nitrogen dioxide, and ozone. While nitrogen dioxide does not exert consistent effects on lung function, ozone, respirable particulate matter, and allergens impair lung function and lead to increased airway responsiveness and bronchial obstruction in predisposed subjects.[62] In addition to acting as irritants, airborne pollutants modulate the allergenicity of antigens carried by airborne particles.[62] Moreover, air pollutants such as diesel exhaust emissions are thought to modulate the immune response by increasing Ig E synthesis, thus facilitating allergic sensitization in atopic subjects and the subsequent development of clinical symptoms.[63]

Geographic variation in the distribution of environmental pollution was the topic of an invited 2001 workshop on Urban Air Pollution and Health Inequities organized by the American Lung Association[64] and a review.[65] There is evidence[66] that some diesel exhaust components can vary substantially across an urban area as a function of traffic volume and type, and road and house characteristics. For example, in a pilot study[66] in Harlem, NY, elemental carbon levels ranged by a factor of four across sites in close proximity to one another, while particulate matter levels < 2.5 μm were quite similar. Elemental carbon levels (measured as black smoke) near major roads in the Netherlands were 2.6 times greater than levels at background sites, vs a factor of 1.3 for particulate matter levels < 2.5 μm.[67] Similarly, polycyclic aromatic hydrocarbon (PAH) concentrations in an urban center differed by a factor of three between measurements on a street and in a park, with traffic contributing an estimated 80% of ambient concentrations.[68] Studies in the Boston area have confirmed this pattern. One study[69] found geometric mean concentrations of 31 ng/m^3 for particle-bound PAHs in an urban location, compared with 8 ng/m^3 in a suburban setting. Another study in the Roxbury area of Boston[70] found strong diurnal variability in PAH concentrations with minimal concentrations in low-traffic hours and significantly higher concentrations with proximity to a major bus terminal. Finally, ultrafine particle concentrations have also been strongly correlated with traffic patterns. In three large European cities, ultrafine particle number concentrations were a factor of 20 greater at peak traffic periods than at night. In a study[71] isolating the effect of a major road in Australia, exposure to submicron-sized particles was a factor of seven greater within 15 m of the road compared with average urban exposure levels. Furthermore, a study[72] in Boston demonstrated an order of magnitude difference in indoor levels of ultrafine particles, even given similar outdoor concentrations, that were related to ventilation and site characteristics.

Health Disparities and Cigarette Smoking

Exposure to tobacco smoke is associated with childhood asthma.[8,42] One study[73] has suggested that mite sensitization is more common among smoke-exposed children. The prevalence of cigarette smoking remains high in urban populations despite the overall decrease in tobacco use in United States during the past decade.[8] Passive exposure to environmental tobacco smoke is also more common in

low-income, urban communities than in other demographic groups. For example, 59% of urban asthmatic children enrolled in the National Cooperative Inner-City Asthma Study[74] and 48% of urban asthmatic children enrolled in the Inner-City Asthma Study[75] live in a house with at least one cigarette smoker. In the National Cooperative Inner-City Asthma Study,[74] a household member was smoking during 10% of the home visits, and 48% of urine samples collected from asthmatic children had cotinine/creatine ratios that were consistent with significant tobacco smoke exposure in the last 24 h.

Notably, smoking behaviors are also socially patterned. Smoking can be viewed as a strategy to cope with negative affect or stress.[73,76,77] Indeed, smoking has been associated with a variety of stressors and types of disadvantage, including unemployment, minority group status, family disorder, violence, as well as depression, schizophrenia, and other psychological problems.[78,79] Stress in particular is associated with adolescent cigarette use,[80] smokers' reported desire for a cigarette, and being unsuccessful at quitting.[81,82]

These relationships among stress and smoking may be considered from a neighborhood perspective as well. Studies[83–85] have demonstrated effects of neighborhood social factors on smoking behavior. It has been hypothesized that neighborhood SES may be related to increased social tolerance and norms supporting behavioral risk factors such as smoking.[86] In adult African-American populations, the prevalence of smoking is higher relative to whites. Evidence from the 1987 General Social Survey suggests that stress may be one factor promoting increased prevalence of smoking in African-American communities.[87] Romano and colleagues[88] surveyed 1,137 African-American households and found that the strongest predictor of smoking was the report of high-level stress, represented by an abbreviated hassles index. The hassles index was a 10-item scale based on items chosen to represent a dimension that community residents perceived to be especially relevant. Among the items were neighborhood-level factors including concern about living in an unsafe area. Threat due to violence in the community has also been linked to an increased risk of smoking in a study performed in Harlem.[89]

Health Disparities in Asthma: Where Do Genetics Fit In?

Asthma is a complex trait that is determined by both genetic and environmental factors. Evidence for genetic predisposition to asthma (and related phenotypes) is derived from family studies, twin studies, adoption studies, and segregation analyses[90] (also see Burkart et al[14] for a more recent review). There is also evidence that different genes influence asthma phenotypes of different racial/ethnic groups.[91] Many candidate genes contributing to the development and expression of asthma have been proposed including gene variants associated with T-cell differentiation and related biological processes (*eg*, cytokine function and IgE production), genes related to drug response (*eg*, β-adrenergic receptor and glucocorticoid receptor), and genes important to the handling of environmental toxins (*eg*, cytochrome P450 and glutathione S-transferase genes). Genetic polymorphisms in the β_2-adrenergic receptor have been linked to asthma severity,[92] and the prevalence of functional polymorphisms in the β_2-adrenergic receptor gene varies across race.[93]

There are a number of key ideas to keep in mind when considering the genetic determinants of asthma disparities. This significant rise in asthma prevalence and severity over the past 2 to 3 decades, along with the widening disparities is too rapid to be explained by changes in genetic factors. Moreover, it needs to be kept in mind that genetic factors generally determine susceptibility to but not development of the disease.[94] Racial-ethnic variability in the distribution of genetic polymorphisms can also modify the response to environmental exposures that are socially and economically patterned as well as the response to drug treatments.[95] As we increasingly come to understand that the concept of "race" is not a true biological characteristic, we need to avoid simplistic interpretations of intergroup differences or genetic stratification.[96–99] That is, although race/ethnicity has been used as a proxy for biology and genetic risk in the past, researchers are increasingly viewing race as more of a social construct. Genetic studies that ignore interactions with broad environmental factors in ethnic minority populations would likely perpetuate the view of race as a biological construct.[100]

It is unlikely then that genetic factors alone explain the rise in asthma prevalence or the observed disparities. It is more likely the case that gene-by-gene and gene-by-environment interactions are the crucial determinants of asthma occurrence and severity. Genetic variants that have causal effects but also modify the host response to social and physical environments may not be unique to minority populations and are likely to be common among the general population. Rather, differential exposure to relevant environmental exposures could explain disease disparities.[101] The examination of the main effects of genes and interactions between genes and environmental factors will more likely inform the discernment of

common final pathways to asthma disparities. From the perspective of health disparities, this means that both the environmental exposure and the genetic factor will be critical determinants in the causation pathway of the disease. Subjects who are exposed to toxins that are more highly prevalent in urban communities (*eg*, stress, smoking, aeroallergens, and diesel exhaust) and carry the genetic variants will have the greatest increased risk of disease, whereas subjects who are exposed to the toxins but do not have the genetic variant will have only a modestly increased risk of disease. Thus, applying genetic knowledge about asthma to reducing asthma disparities will require sophisticated strategies based on the role of both significant genetic and relevant social and physical environmental risk factors. No amount of progress in understanding the genetic factors underlying asthma etiology and response to treatment will help to reduce health disparities unless racial/ethnic/SES disparities in exposure to risk-related social and environmental factors are concomitantly addressed.

Need for a Multilevel Perspective

The etiology of health problems is increasingly recognized as a result of the complex interplay of influences operating at several levels, including the individual, the family, and the community. As part of this growing complexity, evidence supports the notion that connections between health and economic well-being are embedded within the larger context of people's lives.[102,103] The profound question, initially raised in the context of cancer,[104] is, *what* gets asthma? Is it the cell, gene, organ, individual, household, population subgroup, or community? Indeed, the potential answers are rarely exclusive.[104,105]

As reviewed above, more recently observed epidemiologic trends suggest that asthma may provide an excellent paradigm for understanding the role of community-level contextual factors in disease.[100] Specifically, a multilevel approach that includes an ecological perspective may help to explain heterogeneities in asthma expression across socioeconomic and geographic boundaries that to date have remained largely unexplained (Fig 1).

Traditionally, asthma epidemiology has focused on individual-level risk factors and family factors. Far less attention has been given to the broader social context in which individuals live. Although it is beyond the scope of the current discussion given the space limitations, one also must consider the developmental timing of exposures over the course of a lifetime relative to specific asthma outcomes, whether individ-

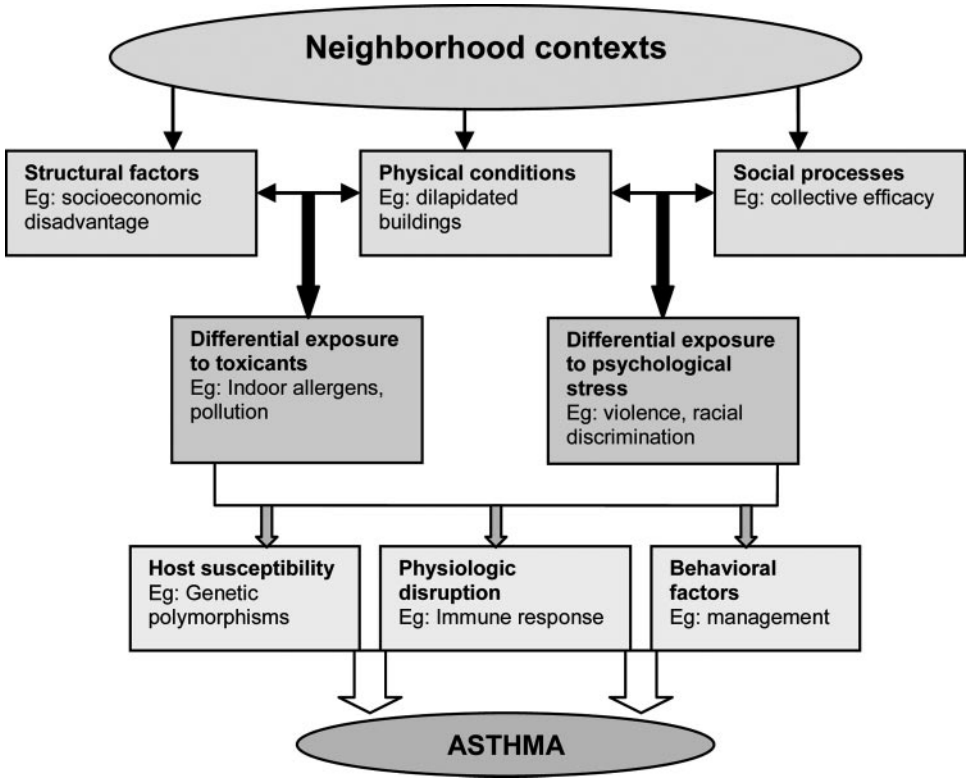

FIGURE 1. A multilevel approach including an ecological perspective to explain heterogeneities in asthma expression across socioeconomic and geographic boundaries.

ual or contextual factors are being considered.[106] Factors leading to the onset, remission, or persistence of asthma across the course of a lifetime may be influenced by physical exposures and social experiences beginning *in utero*, a series of social and biological experiences initiated by early childhood exposure, or cumulative exposure to toxic biological or social factors over critical periods of development.

Could Neighborhood Context Be a Source in Producing Social Disparities in Asthma?

There is evidence that the risk factors associated with asthma, which were outlined earlier, are unevenly distributed across communities and neighborhoods. The failure to view these risk factors within its context can be limiting.[65,107] Neighborhood contexts, defined by their characteristics related to socioeconomic disadvantage, physical conditions, and social processes, may play a critical role in accounting for the social disparities in asthma. Indeed, each of the risk factors (*eg*, exposure to indoor allergens, outdoor pollution, and smoking) that were discussed in the previous sections is likely to be distributed disproportionately across populations as well as communities and neighborhoods. At the same time, there has been growing interest in the potential role of the social environment in both health and psychological processes. This is a useful way to conceptualize environmental influences on health whether one operationalizes the environment as a social or a physical construct. Both physical and social factors can be a source of environmental demands that contribute to the stress experienced by populations living in a particular area.[108] Bridging such theoretical constructs with research into asthma disparities is timely, given the convergence with advances in understanding the influences of psychological stress on the development and expression of asthma.[109,110] Structurally disadvantaged neighborhoods may not only generate clustering of physical risk factors but may also act as a stressor inducing, for instance, individuals to smoke. Neighborhood structural disadvantage may also contribute to the level of sociophysical disorder in the community, including violence,[111,112] which may, in turn, influence asthma, as reviewed in more detail below.[113,114]

The potential import of such a framework stems from a number of observations. Notably, asthma trends are consistent with an inverse association between SES and adverse health outcomes found for many diseases.[115–118] Explanations of such a ubiquitous socioeconomic gradient in health together with the observation that it is capable of replicating itself on new disease processes as they emerge in society calls for an understanding of how humans can become generally vulnerable or resilient to disease over time.[32,119] This argues for the consideration of not only physical factors that alter biological processes but also how psychosocial conditions get into the body. Chronic stress may be a pervasive environmental factor imposed on already vulnerable populations,[108,120] resulting in an enhanced biological response to known physical environmental exposures. Mechanisms linking psychological stress, personality, and emotion to atopic disease continue to be elucidated and have been reviewed elsewhere.[110] Moreover, the effects of environmental toxins (*ie*, air pollution and tobacco smoke) on atopy and asthma may be mediated by the common pathway of oxidative stress, a process that may be potentiated by chronic psychological stress. Further research is needed to examine these relationships.

Ecological views on health recognize that individual-level health risks and behaviors have multilevel determinants, which are in part influenced by the social context within which subjects live.[31] Emerging scholarship on how social environments "get under the skin" to influence health suggests that psychological factors play a key role.[121] That is, the degree of chronic stress is significantly influenced by the characteristics of the families, homes, and communities in which we live. Indicators of neighborhood disadvantage (ND) that may lead to chronic stress have been investigated in relation to urban children's development. ND, characterized by the presence of a number of area-level stressors including poverty, unemployment/underemployment, percentage of unskilled laborers, limited social capital or social cohesion, substandard housing, and high crime/violence exposure rates.[122] Such stress is chronic and can affect all subjects in a given environment regardless of their individual-level risks.[123] In the United States, many urban communities are characterized by high ND levels.[116] Evidence from social epidemiology on the determinants of health disparities among racial and ethnic minorities and low-SES populations points to the powerful influence of community characteristics in promoting health and well-being. One potential mediating feature of community life that has generated considerable attention is the concept of "social capital."[124,125] Social capital, and related constructs such as social cohesion, have been to linked to economic development,[126] investment in public goods such as education,[127] and crime/violence rates in a community.[125]

Our previous work has identified violence exposure as a prevalent factor that concerns residents of Boston communities[128] and, in turn, has linked violence exposure to asthma morbidity.[113,129] Violence serves as a good example of these social processes that may be impacting health. Social capital is strongly correlated with violent crime rates,

which impacts community resilience by undermining social cohesion.[130,131] Thus, crime and violence (or the lack of it) can be used as indicators of collective well-being, social relations, or social cohesion within a community and society.[114] Violent victimization is a major cause of childhood morbidity in urban America. The rates of experiencing and witnessing serious and lethal violence among inner-city youth are also high.[132–135] A prevalence study[136] in a pediatric primary care clinic at Boston City Hospital found that 10% of children had witnessed a knifing or shooting before the age of 6 years; 18% had witnessed shoving, kicking, or punching; and 47% had reported hearing gunshots in their neighborhood. In a preadolescent sample in Boston, our group found that 61% had witnessed shoving, kicking, or punching; 8% had witnessed a stabbing or shooting; and 21% reported hearing gunshots in their communities.[128]

A Multilevel Analytic Approach to Modeling Asthma Disparities

Analyzing variations in asthma and its associated risk factors within its social and neighborhood context requires employing an explicit multilevel analytical strategy. Specifically, these approaches allows researcher to do the following: (1) quantify the extent to which individual asthma gets clustered by neighborhood and community grouping; (2) quantify the extent to which neighborhood variations in asthma are due to the clustering of risk factors along with a possibility to quantify the extent to which the effect of a particular individual risk factor varies from neighborhood to neighborhood; and (3) quantify the relative importance of individual and neighborhood-level exposures in predicting individual asthma. These three constitutive components of a multilevel analytic framework are identified and discussed for asthma-disparities research.[28–30]

Evaluating Sources of Variation: Compositional and/or Contextual

A fundamental application of multilevel methods is disentangling the different sources of variations in asthma. Evidence for variations in asthma, for instance, between different neighborhoods can be due to factors that are intrinsic to, and are measured at, the neighborhood level. In other words, the variation is due to what can be described as contextual, area, or ecological effects. Alternatively, variations between neighborhoods may be compositional (*ie*, certain types of people who are more likely to have asthma due to exposure to certain individual risk factors tend to be clustered in certain places). It is important to note that when individual risk factors account for a neighborhood variation in asthma that it also would suggest that the effects of these risk factors are not purely individual since they are now no longer randomly distributed across neighborhoods and, as such, should be interpreted as the compositional effects of risk factors. The issue, therefore, is not whether variations between different neighborhoods exist (they usually do), but the primary source of these variations. Put simply, are there significant contextual differences in asthma between settings (*eg*, neighborhoods) after taking into account the individual risk factors associated with the patients within the neighborhood?

Describing Heterogeneity in the Influence of Individual Risk Factors

Contextual differences may be complex such that they may not be the same for all types of people. Describing such contextual heterogeneity is another aspect of multilevel analysis and can have two interpretative dimensions. First, there may be a different amount of neighborhood variation, such that, for example, for high-social class individuals the neighborhood they live in may not matter (thus yielding a smaller between-neighborhood variation in asthma), but it may matter a great deal for the low-social class individuals (thus yielding a large between-neighborhood variation). Second, there may be a differential ordering; neighborhoods that are high in asthma prevalence for one group are low for the other and *vice versa*. Stated simply, the multilevel analytical question is are the contextual neighborhood differences in asthma, after taking into account the individual composition of the neighborhood, different for different types of population groups?

Characterizing and Explaining the Contextual Variations

Contextual differences, in addition to people's characteristics, may also be influenced by the different characteristics of neighborhoods. Stated differently, individual differences may interact with context, and ascertaining the relative importance of individual and neighborhood measures is another key aspect of a multilevel analysis. For example, over and above social class (individual characteristic) asthma may depend on the levels of social cohesion of the neighborhoods (neighborhood characteristic). The contextual effect of social cohesion can either be the same for both the high and low social class,

suggesting that while neighborhood social cohesion explains the prevalence of asthma, it does not influence the social class inequalities in asthma within the neighborhood. On the other hand, the contextual effects of social cohesion may be different for different groups. The analytical question of interest is whether the effect of neighborhood-level socioeconomic characteristics on health is different for different types of people. Appendix 1 provides a technical outline of the generic multilevel regression models that could be developed into model asthma disparities.

Future Directions

In this chapter, we make a case to consider the determinants of asthma within an explicitly multilevel and complimentary perspective. While we have made much progress in understanding the role of proximate risk factors in influencing asthma, this research tends to assume that individual risk factors, whether behavioral (*eg*, smoking) or environmental (*eg*, exposure to allergens or stress), are randomly distributed across populations and communities. There is a clear need to understand asthma and its associated risk factors within their social and neighborhood contexts. The observed wide geographic and sociodemographic variation in asthma expression remains a paradox that is largely unexplained by the accepted physical environmental risk factors and has led to reconsideration of the interplay among biological and social determinants in understanding such disparities in the asthma burden.[100] Increasingly, evidence suggests a key role for psychological factors in explaining how social environments "get under the skin" to influence health. Psychological stress may be conceptualized as a social pollutant that, when "breathed" into the body, may disrupt biological systems related to inflammation through mechanisms potentially overlapping with those altered by physical pollutants, allergens, and toxicants.[110] The examination of genetic variants that have causal effects but also modify the host response to relevant social and physical environments will be most likely to inform the discernment of common final pathways to asthma disparities. An understanding of the specific mechanistic pathways that cause asthma therefore has to be intrinsically multilevel.

Technical Appendix

Multilevel statistical approaches[137–141] provide a unifying framework for understanding asthma disparities. We provide a short methodological outline exemplifying three generic models that may have particular relevance for furthering the research agenda focused on asthma disparities that may accommodate the complexities laid out in this manuscript.

Let the binary response, whether an individual has asthma or not (1,0) be y, for individual i living in neighborhood j. For exemplification, we consider one individual risk factor, exposure to allergens, x_{1ij}, coded as 1 if exposed and 0 otherwise, for every individual i in neighborhood j; and a neighborhood predictor, x_{2j}, for the level of social cohesion in neighborhood j, coded as 1 if there is low-level social cohesion and 0 otherwise. The probability that $x_{ij} = 1$ can be denoted by π_{ij}, which in turn is related to a set of individual and neighborhood predictors by $f(\pi_{ij})$, which is a transformation of π_{ij}, with a logit link function such that $f(\pi_{ij}) = \log(\pi_{ij}/[1 - \pi_{ij}])$, where the quantity $\pi_{ij}/(1 - \pi_{ij})$, is the log odds that $y_{ij} = 1$.

We can quantify the extent to which there is neighborhood-level clustering in asthma by calibrating the following model:

$$\text{logit}(\pi_{ij}) = \ln \frac{\pi_{ij}}{(1 - \pi_{ij})} = \beta_0 + \beta_1 x_{1ij} + u_{0j} \qquad (1)$$

where $\text{logit}(\pi_{ij})$ is the linear predictor consisting of a fixed part of a fixed part $\beta_0 + \beta_1$ and a random part u_{0j}. The parameter β_0 will estimate the log odds of having asthma for the reference group, with no exposure to allergens, and the parameter β_1 will estimate the differential in the log odds of having asthma for individuals exposed to allergens. The parameter u_{0j}, meanwhile, represents the random differential for neighborhood j that is assumed to have an independent and identical distribution: $u_{0j} \sim N(0,\sigma^2_{u0})$. The random parameter σ^2_{u0} is the between-neighborhood variation in the log odds of having asthma, which is conditional on the relationship between the log odds of having asthma and individual risk factors.

The neighborhood heterogeneities that are attributable to the observable risk factors measured at the individual level can be assessed, with some fraction of the remaining residual neighborhood heterogeneities indicative of contextual processes. Indeed, if the neighborhood variation in asthma decreases after taking into account the measured individual risk factors, that would also suggest that these risk factors are not randomly, but disproportionately and systematically, distributed across neighborhoods. This also raises the question of interpreting the effects of these risk factors as purely individual. Instead, they suggest a compositional effect of risk factors.

The model in equation 1 can be extended to then evaluate the extent to which the fixed-effect individual risk factors vary across neighborhoods. Evidence for neighborhood heterogeneity in the impact of individual risk factors would suggest the need to consider individual risk factors within their context. This model would then take the following form:

$$\text{logit}(\pi_{ij}) = \ln \frac{\pi_{ij}}{(1 - \pi_{ij})} = \beta_0 + \beta_1 x_{1ij} + u_{0j} + u_{1j} x_{1ij} \qquad (2)$$

Representing the between-neighborhood differences in equation 2 are now two terms, (u_{0j},u_{1j}), associated with the constant and x_{1ij}, respectively. Making the usual IID assumptions, the neighborhood differences at level 2 can be summarized through a variance-covariance parameter matrix consisting of two variances, (σ^2_{u0}) and (σ^2_{u1}), and one covariance, (σ_{u0u1}), respectively. If supported by the data, a statistically significant variance-covariance matrix would suggest neighborhood heterogeneity in the ways in which individual risk factors impact on asthma. Meanwhile, the level-2 variance-covariance coefficients can be used to derive neighborhood-specific predictions, usually referred to as *posterior residuals*, thereby allowing the researcher to make neighborhood-specific inferences.

While the model in equation 2 provides a basis to perhaps

suggest that neighborhood matters for asthma (in some complex way), it does not tell us what it is about neighborhoods that is important for asthma. Thus, for instance, x_{2j}, representing low levels of neighborhood social cohesion, can be introduced to account for the observed neighborhood variation equation, σ^2_{u0}, σ^2_{u1}, and one covariance, σ_{u0u1}, from model 2, in addition to quantifying the predictive power of neighborhood social cohesion on the individual probability of having asthma, such that there are differential effects of neighborhood social cohesion depending on the individual's exposure to allergens:

$$\text{logit}(\pi_{ij}) = \ln \frac{\pi_{ij}}{(1 - \pi_{ij})} = \beta_0 + \beta_1 x_{1ij} + \beta_2 x_{2j} + \beta_3 x_{2j} \cdot x_{1ij} + u_{0j} + u_{1j} x_{1ij} \quad (3)$$

The parameter of interest in this model would be β_2 and β_3, which would estimate the risk associated with living in neighborhoods with social cohesion on asthma for the two groups that are exposed and unexposed to allergens. If there is a statistically significant support for an association between neighborhood social cohesion and the individual probability of having asthma, then we would expect the neighborhood variance-covariance parameters to reduce toward zero.

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